# **REMARKS**

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

# Summary of Telephonic Interview

Applicants kindly thank Examiner Zarek, as well as his colleague, for providing their time and helpful suggestions during the telephonic interview of September 22, 2009.

During the interview, the rejections of record were discussed. Initially, Applicants proposed amending the claims to define the patient population as a patient with low-HDL cholesterolemia or arteriosclerosis. The Examiners indicated that this amendment should address the issue presented in the rejection under 35 U.S.C. § 112, second paragraph.

Additionally, Applicants proposed amending the claims to delete "probucol bisphenol". The Examiners indicated that this amendment should be helpful in overcoming the prior art rejections based on Stocker.

The Examiners suggested that Applicants provide comments regarding the unobviousness of probucol spiroquinone and probucol diphenoquinone, in view of the known metabolism of probucol. Applicants appreciate the Examiners' suggestion, and provide such comments below.

The Examiners also requested that Applicants spell out "ABCA1" in its first instance in claim 6.

Applicants appreciate the Examiners' kind assistance in advancing prosecution of this application.

#### Claim Amendments

Claim 6 has been amended to delete "probucol bisphenol", to define the patient population as a "patient with low-HDL cholesterolemia or arteriosclerosis", and to spell out ABCA1 in its first instance. Support for these amendments is found on page 1, lines 7-8 and 20-23 of the specification.

Claim 7 has been amended to be consistent with claim 6.

# Rejection Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 6 and 7 under 35 U.S.C. § 112, second paragraph, has been rendered moot in view of the above-discussed claim amendments. Accordingly, it is respectfully requested that the above-rejection be withdrawn.

# Patentability Arguments

The patentability of the present invention over the disclosure of the reference relied upon by the Examiner in rejecting the claims will be apparent upon consideration of the following remarks.

### Rejection Under 35 U.S.C. § 102(b)

Claim 6 is rejected under 35 U.S.C. § 102(b) as being anticipated by Stocker (WO 02/04031). Applicants respectfully traverse this rejection.

#### The Position of the Examiner

The Examiner takes the position that Stocker teaches a method of administering chow containing probucol bisphenol to mice. The Examiner asserts that oral administration of probucol bisphenol would inherently increase ABCA1 expression.

# Applicants' Arguments

As discussed above, Applicants' amended claims exclude probucol bisphenol. Stocker fails to teach a method for increasing expression of ABCA1 comprising administering a therapeutically effective amount of **probucol spiroquinone or probucol diphenoquinone** to a patient with low-HDL cholesterolemia or arteriosclerosis. Therefore, Stocker fails to teach each and every limitation of Applicants' claim, as is required for anticipation.

Accordingly, it is respectfully requested that the above-rejection be withdrawn.

# Rejection Under 35 U.S.C. § 103(a)

Claim 7 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Stocker. Applicants respectfully traverse this rejection.

# The Position of the Examiner

The Examiner takes the position that it would have been obvious to one of ordinary skill in the art to combine probucol bisphenol and an antithrombic drug.

### Applicants' Arguments

As discussed above, Stocker fails to teach each and every limitation of Applicants' amended claim 6. Claim 7 depends directly on claim 6, and thus is patentable for the reasons discussed above.

Additionally, Stocker fails to suggest the method recited in Applicants' amended claims. Specifically, Stocker fails to teach or suggest a method for increasing expression of ABCA1 comprising administering a therapeutically effective amount of **probucol spiroquinone or probucol diphenoquinone** to a patient with low-HDL cholesterolemia or arteriosclerosis.

The following description is found on page 2 of Applicants' specification.

"However, probucol also has a clinically disadvantageous effect, i.e., reduces the cholesterol level in the HDL fraction... unlike other lipid-lowering agents which have the reaction properties in LDL such as statins or fibrates (for example, refer to Non-Patent Documents 1 and 2).... It is thought that this reduction in HDL-cholesterol is due to functional inhibition of ABCA1 (for example, refer to Non-Patent Documents 3, 4, and 5)."

(Please see Appendices 1 and 2, attached hereto.)

From the above description in Applicants' specification, it is apparent that probucol has been known to "lower HDL", because of its <u>functional inhibition of ABCA1</u>.

On the contrary, probucol spiroquinone (SQ) and probucol diphenoquinone (DQ) exert the efficacy of "<u>elevating HDL</u>" by virtue of inhibiting the degradation of ABCA1 (the increase in ABCA1 levels).

Thus, even though SQ and DQ are metabolites, derived from probucol, the biological

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actions of SQ and DQ are completely contrary to those exerted by probucol.

Therefore, Applicants respectfully assert that the biological actions of SQ and DQ would not have been obvious to one of ordinary skill in the art, based on the teachings of Stocker, even

taking into consideration the known metabolism of probucol.

Applicants also refer to the Examiner to the remarks set forth on pages 5 and 6 of

Applicants' response filed May 18, 2009. A copy of these pages is attached hereto as Appendix

3, with emphasis, for the Examiner's convenience.

In view of the above, it is evident that the subject matter of Applicants' amended claims 6

and 7 is clearly patentable over the teachings of Stocker. It is respectfully requested that this

rejection be withdrawn.

Conclusion

Therefore, in view of the foregoing amendments and remarks, it is submitted that each of

the grounds of rejection set forth by the Examiner has been overcome, and that the application is

in condition for allowance. Such allowance is solicited.

If, after reviewing this Amendment, the Examiner feels there are any issues remaining

which must be resolved before the application can be passed to issue, the Examiner is

respectfully requested to contact the undersigned by telephone in order to resolve such issues.

Respectfully submitted,

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